UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,097	06/14/2001	Anton Wellstein	38596.0005	3830

25227 7590 06/06/2005

MORRISON & FOERSTER LLP
1650 TYSONS BOULEVARD
SUITE 300
MCLEAN, VA 22102

EXAMINER	
KOLKER, DANIEL E	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/880,097	WELLSTEIN, ANTON	
	Examiner	Art Unit	
	Daniel Kolker	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *95 - 118* is/are pending in the application.

4a) Of the above claim(s) *106-118* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *95-105* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3/16/05 5/2/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 16 March 2005 has been entered. Applicant has canceled claims 1 – 94 and added new claims 95 – 118. Claims 95 – 118 are now pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

3. On page 5 of the remarks filed 16 March 2005, applicant requests rejoinder of claims 106 – 118 in accordance with *In re Ochiai* practice. Applicant is advised that the pending product claims (claims 95 – 105) are not currently in condition for allowance for the reasons set forth in this Office action and therefore methods claims will not be rejoined at this time.

4. Claims 106 – 118 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2 February 2004.

Claims 95 – 105 are under examination in the current Office action.

Information Disclosure Statement

The reference cited on the Information Disclosure Statement filed 2 May 2005 has been considered but is not in proper format for publication on the face of a patent.

Reference 18 on the Information Disclosure Statement filed 16 March 2005 has been considered but is not in proper format for publication on the face of a patent.

Withdrawn Rejections and Objections

The following rejections made in the previous office action are withdrawn:

5. The rejection of claims 80, 81, 90, 91, 93, and 94 under 35 USC 112, second paragraph. Applicant has canceled the claims, and new claims 95 – 105 refer to a specific GenBank accession number, obviating the rejection.

6. The rejection of claims 10 – 17, 21 – 23, 69 – 94 under 35 USC 112, first paragraph for lack of enablement over the full scope of the claims. On page 3 of the previous Office action the examiner acknowledged that the specification was enabling for the extracellular domain (ECD) of human ALK. The new claims do not recite any of the language that the examiner had considered non-enabled, specifically variants, fragments, or peptido-mimetics. The new claims are limited to specific residues of a specific sequence.

7. The rejection of claims 1 – 22 and 69 – 94 under 35 USC 102 as being anticipated by Iwahara. Applicant has amended the claims such that they now exclude the full-length extracellular domain, and Iwahara et al. teach that their molecule included the full-length extracellular domain (see p. 440, second column).

Claim Rejections - 35 USC § 112

8. Claims 95 – 105 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988).

Claims 95, 99, 104, and 105 recite "PTN", which is defined in claim 95 as pleiotrophin. The specification discloses (p. 18 lines 1 – 5) that a pleiotrophin molecule was used to isolate ALK. The specification does not disclose what species that pleiotrophin was from, and the term is limited by name only and not by structure. The only functional definition provided in claim 95 is that pleiotrophin binds to ALK. It is acknowledged that there is considerably homology across species for full-length pleiotrophin. Weber et al. (2000. Cancer Research 60:5284 – 5288) teach that human, mouse, and rat PTN are identical and have a molecular weight of 18,000 (page 5284, second column, first complete paragraph). However, the claim as currently written includes anything called PTN. The art teaches a truncated form of mouse PTN, which has only

the first 40 of the usual 168 amino acids, is still called PTN (see Zhang et al., 1999. Proc Natl Acad Sci USA 96:6734 - 6738.) The specification discloses that across certain species there is sequence conservation (see paragraph spanning pp. 7 – 8) but neither the claims nor the specification indicate what that sequence is. The claims appear to have no structural limitation with respect to PTN. A skilled artisan would have to resort to undue experimentation to test whether the claimed polypeptides bind to the broad genus of molecules called pleiotrophin.

The nature of the invention, polypeptides which bind to other polypeptides, is complex. The claims are broad, as detailed above. The art indicates that acceptable definitions of PTN include those truncated proteins which comprise less than half of the full-length protein. There is no guidance in the specification as to how to choose a PTN molecule to determine if it can bind to the claimed extracellular domain of ALK, and there is no requirement in the claim that any particular residues of PTN bind to the instantly claimed ALK fragment. Because the structure is not recited in the claim or defined in the specification, it would not be possible for a skilled artisan to replicate the experiments described herein. Therefore, a skilled artisan would have to resort to undue experimentation to make and use the invention as claimed.

9. Claims 95 – 105 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 95, 99, 104, and 105 recite "PTN", which is defined in claim 95 as pleiotrophin. The specification discloses, on the paragraph spanning pp. 7 – 8, that this molecule is expressed in several species. While the specification also discloses that there is a certain degree of sequence conservation across species, *it does not indicate what the common core structure is.* Pleiotrophin is a broad genus, and while the specification indicates that applicant was in possession of one form of ALK that can bind one form of PTN, applicant has not disclosed a reasonable number of examples of the entire genus to allow the public to conclude that he was in possession of ALK that can bind to any form of PTN. The state of the prior art indicates that PTN includes, for example, full-length PTN as well as fragments. For example, Weber et al. teach that mouse, rat and human PTN are identical and have a molecular weight of 18,000 (see p. 5284, second column, first complete paragraph). However, Zhang et al. teach that a molecule that comprises only 40 of the usual 168 amino acids is still PTN. Pleiotrophin,

as defined in the art, clearly includes both the 40-residue peptide and the 168-residue peptide. The specification does not provide support for the entire genus.

10. Claims 95 –105 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 95 recites GenBank accession number U66559 and refers to amino acid residues therein. This is a nucleic acid sequence, not a protein sequence, and thus reference to specific amino acid residues are indefinite, as there are no amino acid residues. Furthermore, it is unclear whether the residue numbers recited in the claim refer to residues of a full-length protein or of a mature protein, i.e. without the signal sequence. In the absence of a specific reference sequence, residue numbers themselves are meaningless.

Furthermore claim 103 is considered indefinite because it recites the term "therapeutically effective amount" but neither this claim, nor the base claim, nor the specification provide guidance as to what this amount is to be effective for. A skilled artisan would not be able to determine the metes and bounds of this claim, as there is no guidance as to what the amount should be effective in doing.

Claim 105 is also considered indefinite because it recites "a test substance". This term could be anything, as any substance could be tested. The preamble of the claim is not drawn to testing, and it is unclear and confusing as to what is being tested. A skilled artisan could not determine the metes and bounds of this claim, because it is unclear what substances, molecules, or compositions of matter constitute "a test substance".

Claim Rejections - 35 USC § 102

11. Claims 95 – 99, 101, and 104 are rejected under 35 U.S.C. 102(b) as being anticipated by Aigner et al. (March 1999, Proceedings of AACR, cited by applicant on the information disclosure statement filed 20 July 2004). The claims are drawn to a polypeptide that comprises a portion of ALK and binds to PTN. Dependent claims are drawn to specific properties of the compound (claims 96 – 98) or the compound bound to PTN.

Aigner et al. teach a polypeptide that binds to PTN. It is acknowledged that Aigner et al. are silent as to the sequence, or even the name of this polypeptide. However, Aigner et al. used the same starting material (human fetal brain cDNA library), the same technique (panning phage-display, with recombinant PTN as bait), and the instant inventor is one of the authors on

the reference by Aigner et al. Absent clear evidence to the contrary, it is assumed that the molecule isolated by Aigner et al. is in fact the same molecule as that instantly claimed. Therefore the teachings of Aigner et al. are considered to be relevant. Aigner et al. teach that the binding activity is contained in the extracellular domain of a tyrosine kinase receptor, meeting the limitation of claims 95 and 98. Because the tyrosine kinase domain is completely contained within the intracellular portion of the protein (see Figure 1A of the specification; note that TK (tyrosine kinase) is contained within ICD (intracellular domain) of ALK), and Aigner et al. teach that the receptor fragment which binds PTN is in the extracellular domain, the teachings of Aigner also meet the limitation of claim 96. Claim 97 is drawn to a soluble peptide; this is an inherent property of the peptide itself and cannot be separated from it. Claim 101 is drawn to a composition comprising the polypeptide; since the peptide was contained within phages, the teachings of Aigner et al. meet the "composition" limitation of claim 101. Page 18, lines 5 – 7 of the specification discloses that the technique used in isolating the molecule results in phages which bind to PTN, meeting the limitations of claim 99 and 104.

12. Claims 95 – 98 are rejected under 35 U.S.C. 102(b) as being anticipated by Morris et al. (U.S. Patent 5,770,421, cited by applicant on the information disclosure statement filed 20 July 2004). Morris et al. teach amino acids 27 – 1030 of the human ALK polypeptide (see column 101, claim 5). Morris et al. teach that the extracellular domain of human ALK comprises the first 1030 residues of the peptide, including the signal sequence (see column 26 lines 62 – 66). The peptide taught and claimed by Morris et al. in claim 5 of the '421 patent meets the limitations of claims 95 and 98 because it is the same receptor as instantly claimed (ALK), derived from the same species (human), comprises the relevant amino acids, and does not include the entire extracellular domain, as defined at column 26 lines 62 – 66 of Morris. While Morris et al. did not test for the ability to bind PTN, since the molecule taught by Morris is the same as that instantly claimed it is assumed to inherently have that property. Morris et al. also teach that the tyrosine kinase domain is downstream of the extracellular domain (see Figure 3A, and column 5, lines 37 – 39); therefore the protein taught and claimed by Morris et al. meets the limitation of claim 96, as it lacks the tyrosine kinase domain. Morris et al. also teach removing insoluble matter during the purification of their protein (see column 32 lines 10 – 24), and therefore since it is not insoluble it is, by definition, soluble, and meets the limitation of claim 97. Furthermore Morris et al. teach the

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 95 and 100 - 102 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Aigner et al. in view of Ausbel et al. (1997. Short Protocols in Molecular Biology, pp. 10.82 – 10.84 and 11.23 – 11.25), or in the alternative Morris et al. in view of Ausbel et al. Claim 100 is drawn to the polypeptide of claim 95 immobilized on a surface. Both Aigner et al. and Morris et al. teach polypeptides that comprise a portion but not all of the extracellular domain of ALK, as described in detail in the rejections under 35 USC 102 above. Neither Aigner nor Morris teach immobilization of the peptide of a surface, nor pharmaceutically acceptable carriers in compositions.

Ausbel et al. teach transferring proteins to PVDF membranes. The specific conditions of the transfer are provided on p. 10.84, step 14. Ausbel et al. teach that this is part of a protocol to determine the amino acid sequences; the title of this protocol is "Determination of amino acid sequence of samples on PVDF membranes". It would have been obvious to one of ordinary skill in the art to put the polypeptides of either Aigner or Morris on a PVDF membrane, as taught by Ausbel et al., with a reasonable expectation of success. A motivation to do so would be to sequence the proteins, which is useful to develop drug targets.

Furthermore Ausbel et al. also teach pharmaceutically acceptable carriers for immunization. On pp. 11.23 – 11.25, Ausbel et al. teach methods of immunizing rabbits and indicate that the method is general and can be performed with either native protein antigen or a peptide-carrier protein conjugate (see p. 11.23). The compositions used by Ausbel et al. are PBS (p. 11.23), complete Freund's adjuvant (p. 11.24, step 1), and incomplete Freund's adjuvant (p. 11.24, step 3). These are deemed to be pharmaceutically acceptable, as they are administered to mammals. It would have been obvious to one of ordinary skill in the art to make a composition comprising a pharmaceutically acceptable carrier with the protein from either Aigner or Morris, with a reasonable expectation of success. A motivation to do so would be to immunize rabbits to make antibodies, and is the motivation provided by Ausbel.

Conclusion

15. No claim is allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel E. Kolker
May 27, 2005

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600